

REMARKS/ARGUMENTS

Claims 11-39 are pending.

Claims 1-10 have been cancelled.

Claims 26-39 are withdrawn.

Applicants wish to thank Examiner Weddington for the meeting on October 3, 2007.

The subject of the meeting included all rejections. The applicants' representative pointed out that the supplemental drugs of claim 23 are sufficiently described at pages 52-54 of the specification. We further discussed the rejection under 35 U.S.C. 102(e) over Arkinstall and the obviousness rejection over a number of co-pending applications. The Examiner indicated a willingness to reconsider the rejections.

Claim 23 is rejected under 35 U.S.C. 112 ¶1 for lack of written description.

Claim 23 is directed to a method for treating a metabolic disorder mediated by insulin resistance or hyperglycemia wherein a combination of a compound of formula (1) and a drug selected from the group consisting of an aldose reductase inhibitor, an alpha-glucose inhibitor, a sulfonyl urea agent, a biguanide, a thiazolidine, a PPARs agonist, and GSK-3 inhibitor is administered.

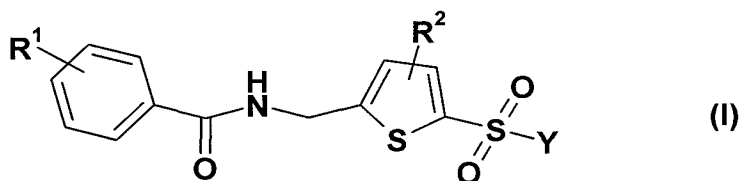
The specification describes a pharmaceutical composition for treatment of a metabolic disorder comprising a compound of formula (1) and at least one supplemental drug. The supplemental drugs are known compounds (see pages 53-56). The specification describes a variety of known aldose reductase inhibitors used in combination with the compounds of formula (1) (see page 53-56, e.g., aldose reductase inhibitors a-x). The specification further describes known alpha-glucose inhibitors (e.g., miglitol and acarbose), sulfonyl urea agents (e.g., glipizide, Glyburide Clorpropamide, Tolbutamide, Tolazamide, and Glimepiride), biguanides (e.g., metformin), and thiazolidines (e.g., piglitazone, rosiglitazone) (see pages 53-56 of the specification). The fact that some biguanides exhibit some toxicity is irrelevant to

written description under 35 U.S.C. 112 ¶1. Biguanides with known activities are described in the specification.

Thus, the specification provides a sufficient description of a representative number of species for each group of a supplemental drug of claim 23. Applicants request that the rejection be withdrawn.

The rejection of claims 11-22 and 25 under 35 U.S.C. 102(b) over Arkinstall, EP 1 088 821, in view of Bennett, *Curr. Opin. Pharmacol.*, 3(4):420-425 (2003), is untenable because (1) Arkinstall does not describe selecting the claimed compounds for treating a metabolic disorder mediated by insulin resistance or hyperglycemia, (2) the compounds of Arkinstall do not necessarily treat metabolic disorders (e.g., diabetes II) when used as Arkinstall teaches, and (3) Arkinstall does not enable for treating a metabolic disorder mediated by insulin resistance or hyperglycemia.

Claim 11 is directed to a method for treating a metabolic disorder mediated by insulin resistance or hyperglycemia comprising administering at least one sulfonamide derivative of the following formula (I):



Arkinstall describes generic compounds broadly encompassing the sulfonamide compounds claimed. Arkinstall discloses that the JNK signaling pathway is implicated in cell proliferation and could play an important role in autoimmune diseases [0010]. Arkinstall shows that the disclosed generic compounds modulate the JNK pathway as JNK inhibitors,

notably JNK2 and JNK3, and are useful for the treatment of the immune and neuronal system disorders [0107], [0135]-[0140]. Arkinstall does not teach selecting specific (e.g., claimed in this application) sulfonamide derivatives and using the selected derivatives for treating other JNK mediated disorders, i.e., a metabolic disorder mediated by insulin resistance or hyperglycemia.

Although Bennett discloses that one JNK inhibitor (CC105 small molecule) has potential in treating insulin resistance and obesity, it does not mean that all Arkinstall compounds of general formula I are necessarily effective for treating metabolic disorder (e.g., diabetes II), i.e., all Arkinstall compounds would not inherently treat metabolic disorders. In fact, the Arkinstall compounds having, for example, X=S are not claimed in this application, and may or may not be effective for the treatment of metabolic disorders.

Bozyczko-Coyne, Curr. Drug Target – CNS & Neurol. Disorders, 1:31-49, 42-43 (2002), shows that the JNK pathway is very complex, involves many levels of regulations, genes, proteins, and disorders. The JNK pathway is implicated in a large number of physiological and pathological functions. See Bozyczko-Coyne, at 43-43. Moreover, the complexity of the organization and regulation at all levels within the JNK signaling cascade continues to evolve. Further, because of the complex cross talk within this signaling cascade as well as its cell type and response specific modulation, it is difficult to predict potential adverse events that might arise from pathway inhibition (Bozyczko-Coyne, page 43). Owing to the breadth of physiological functions mediated via signaling through the JNK family, direct inhibition at the level of the JNK could prove to have liabilities (Bozyczko-Coyne, page 31. right col.).

Therefore, Bennett at best suggests to try the JNK inhibitors for treatment diabetic disorder (one of many disorders modulated via the JNK pathway), but does not support the conclusion that all Arkinstall compounds do treat a metabolic disorder.

The Arkinstall compounds display inhibitory activity of the JNK pathway. However, Arkinstall only describes using the compounds for treating disorders of the autoimmune and neuronal system, see [0001], [0017], and [0135]-[0140]. Arkinstall does not enable treating all disorder related to the inhibition of the JNK pathway. Arkinstall does not provide sufficient nexus between autoimmune and neuronal disorders and metabolic disorders so that they are substantially related and can be treated with the same compounds.

In contrast, this specification describes using the claimed compounds in *in vivo* assay in db/db mice to determine anti-diabetic effect of the test compounds in a model of postprandial glycemia (page 60-61). The experiment on pages 60-61 shows that the blood glucose level and blood insulin were decreased in the treated animals compared to the untreated animals.

Applicants request that the rejection be withdrawn.

Claims 11-25 are rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-36 of co-pending application 10/070,954; claims 1-27 of application 10/088,074; claim 1 of application 10/088,090; claims 1-8 and 14 of application 10/381,197; claims 1-8 and 14 of application 10/381,200; claims 1-10, 12, and 16 of application 10/381,665; and claim 1-11 and 17 of application 10/484,744.

The claims of application 10/088,074 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '074 are useful for treating diseases of the autoimmune and neuronal system. The appl. '074 does not disclose that the sulfonyl hydrazide compounds are effective for treating a metabolic disorder. The appl. '074 does not provide sufficient nexus between autoimmune and neuronal disorders and metabolic disorders so that they are substantially related and can be treated with the same compounds. Further, the appl. '074 does not suggest selecting the specific compounds claimed in this application as the compounds for treating a metabolic disorder.

Also, the appl. '074 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claimed compounds of applications 10/088,090 and 10/381,197 are different from those claimed in this application. Applicants request that the rejection be withdrawn.

The claims of application 10/381,200 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '200 are useful for treating diseases of the autoimmune and neuronal system. The appl. '200 does not disclose that the sulfonyl hydrazide compounds are effective for treating a metabolic disorder. The appl. '200 does not provide sufficient nexus between autoimmune and neuronal disorders and metabolic disorders so that they are substantially related and can be treated with the same compounds. Also, the appl. '200 does not suggest selecting the specific compounds claimed in this application as the compounds for treating a metabolic disorder. Also, the appl. '200 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claims of application 10/381,665 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '665 are useful for treating disorders modulated by abnormal expression of JNK, wherein the disorder is autoimmunity, ischemia or reperfusion. The appl. '665 does not disclose that the sulfonyl hydrazide compounds are effective for treating a metabolic disorder (one of many disorder modulated by the JNK pathway). The appl. '665 does not provide sufficient nexus between autoimmunity, ischemia or reperfusion and metabolic disorders claimed in this application so that they are substantially related and can be treated with the same compounds. Also, the appl. '665 does not suggest selecting the specific compounds claimed in this application as the compounds for treating a metabolic disorder. Also, the appl. '665 does not

enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claims of application 10/484,744 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '744 are useful for treating apoptosis related disorder (e.g., cancer), inflammations, and cardiovascular disorders. The appl. '744 does not disclose that the sulfonyl hydrazide compounds are effective for treating a metabolic disorder. The appl. '744 does not provide sufficient nexus between, for example, apoptosis related disorders and inflammation, and metabolic disorders so that they are substantially related and can be treated with the same compounds. Also, the appl. '744 does not suggest selecting the specific compounds claimed in this application as the compounds for treating a metabolic disorder. Also, the appl. '744 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

The claims of application 10/070,954 are directed to a generic sulfonyl hydrazide compound comprising the species claimed in this application. The compounds of the appl. '954 are used for treating diseases associated with the abnormal expression or activity of JNK. The appl. '954 does not disclose that the sulfonyl hydrazide compounds are effective for treating of all JNK mediated disorders, and specifically, a metabolic disorder. Also, the appl. '954 does not suggest selecting the specific compounds claimed in this application as the compounds for treating a metabolic disorder. Also, the appl. '744 does not enable for treating all disorder related to the inhibition of the JNK pathway. Applicants request that the rejection be withdrawn.

Application No. 10/571,466  
Reply to Office Action of August 24, 2007

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

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